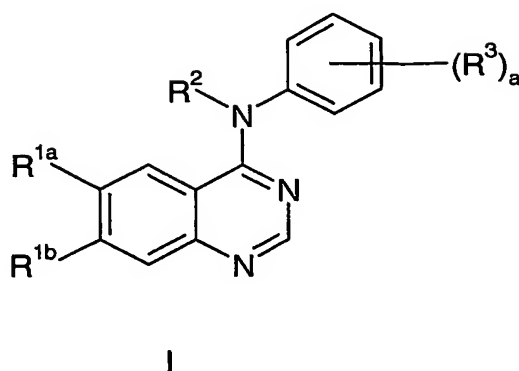


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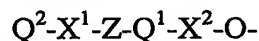
CLAIMS

1. A quinazoline derivative of the Formula I:



wherein:

one of R¹ᵃ or R¹ᵇ is a group of sub-formula (i)



(i)

- 10 where X² and X¹ are independently selected from a direct bond or a group $-[CR^4R^5]_m$, wherein m is an integer from 1 to 6,

Z is C(O), SO₂, -C(O)NR¹⁰-, -N(R¹⁰)C(O)-, -C(O)O- or -OC(O)- where R¹⁰ is hydrogen or (1-6C)alkyl,

and each of R⁴ and R⁵ is independently selected from hydrogen, hydroxy, (1-4C)alkyl,

- 15 halo(1-4C)alkyl, hydroxy (1-4C)alkyl, (1-4C)alkoxy(1-4C)alkyl, or R⁴ and R⁵ together with the carbon atom(s) to which they are attached form a (3-7)cycloalkyl ring, provided that when a group R⁴ or R⁵ is hydroxy, m is at least 2 and the carbon atom to which the hydroxy group is attached is not also attached to another oxygen or a nitrogen atom;

Q¹ is (3-7C)cycloalkylene or heterocyclyl group, which is optionally substituted by one or

- 20 two substituents selected from halogeno, trifluoromethyl, trifluoromethoxy, cyano, nitro, hydroxy, amino, carboxy, carbamoyl, acryloyl, (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl, (1-6C)alkoxy, (2-6C)alkenyloxy, (2-6C)alkynyloxy, (1-6C)alkylthio, (2-6C)alkenylthio, (2-6C)alkynylthio, (1-6C)alkylsulfinyl, (2-6C)alkenylsulfinyl, (2-6C)alkynylsulfinyl, (1-6C)alkylsulfonyl, (2-6C)alkenylsulfonyl, (2-6C)alkynylsulfonyl, (1-6C)alkylamino,
- 25 di-[(1-6C)alkyl]amino, (1-6C)alkoxycarbonyl, N-(1-6C)alkylcarbamoyl, N,N-di-[(1-6C)alkyl]carbamoyl, (2-6C)alkanoyl, (2-6C)alkanoyloxy, (2-6C)alkanoylamino,

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- N-(1-6C)alkyl-(2-6C)alkanoylamino, sulfamoyl, N-(1-6C)alkylsulfamoyl, N,N-di-[(1-6C)alkyl]sulfamoyl, (1-6C)alkanesulfonylamino, N-(1-6C)alkyl-(1-6C)alkanesulfonylamino, carbamoyl(1-6C)alkyl, N-(1-6C)alkylcarbamoyl(1-6C)alkyl, N,N-di-[(1-6C)alkyl]carbamoyl(1-6C)alkyl, 5 sulfamoyl(1-6C)alkyl, N-(1-6C)alkylsulfamoyl(1-6C)alkyl, N,N-di-[(1-6C)alkyl]sulfamoyl(1-6C)alkyl, (2-6C)alkanoyl(1-6C)alkyl, (2-6C)alkanoyloxy(1-6C)alkyl, (2-6C)alkanoylamino(1-6C)alkyl, N-(1-6C)alkyl-(2-6C)alkanoylamino(1-6C)alkyl and (1-6C)alkoxycarbonyl(1-6C)alkyl; Q^2 is an aryl or heteroaryl group, said aryl or heteroaryl group being optionally substituted by
- 10 one of more substituents selected from halogeno, trifluoromethyl, trifluoromethoxy, cyano, nitro, hydroxy, amino, carboxy, carbamoyl, acryloyl, (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl, (1-6C)alkoxy, (2-6C)alkenyloxy, (2-6C)alkynyloxy, (1-6C)alkylthio, (2-6C)alkenylthio, (2-6C)alkynylthio, (1-6C)alkylsulfinyl, (2-6C)alkenylsulfinyl, (2-6C)alkynylsulfinyl, (1-6C)alkylsulfonyl, (2-6C)alkenylsulfonyl, (2-6C)alkynylsulfonyl, 15 (1-6C)alkylamino, di-[(1-6C)alkyl]amino, (1-6C)alkoxycarbonyl, N-(1-6C)alkylcarbamoyl, N,N-di-[(1-6C)alkyl]carbamoyl, (2-6C)alkanoyl, (2-6C)alkanoyloxy, (2-6C)alkanoylamino, N-(1-6C)alkyl-(2-6C)alkanoylamino, sulfamoyl, N-(1-6C)alkylsulfamoyl, N,N-di-[(1-6C)alkyl]sulfamoyl, (1-6C)alkanesulfonylamino, N-(1-6C)alkyl-(1-6C)alkanesulfonylamino, carbamoyl(1-6C)alkyl, 20 N-(1-6C)alkylcarbamoyl(1-6C)alkyl, N,N-di-[(1-6C)alkyl]carbamoyl(1-6C)alkyl, sulfamoyl(1-6C)alkyl, N-(1-6C)alkylsulfamoyl(1-6C)alkyl, N,N-di-[(1-6C)alkyl]sulfamoyl(1-6C)alkyl, (2-6C)alkanoyl(1-6C)alkyl, (2-6C)alkanoyloxy(1-6C)alkyl, (2-6C)alkanoylamino(1-6C)alkyl, N-(1-6C)alkyl-(2-6C)alkanoylamino(1-6C)alkyl and (1-6C)alkoxycarbonyl(1-6C)alkyl, 25 and wherein any (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl and (2-6C)alkanoyl substituent on Q^1 or Q^2 optionally bears one or more substituents (for example 1, 2 or 3) which may be the same or different selected from halogeno, hydroxy and (1-6C)alkyl and/or optionally a substituent selected from cyano, nitro, carboxy, (2-8C)alkenyl, (2-8C)alkynyl, (1-6C)alkoxy, hydroxy(1-6C)alkoxy, (1-4C)alkoxy(1-6C)alkoxy, (2-6C)alkanoyl, 30 (2-6C)alkanoyloxy and NR^aR^b , wherein R^a is hydrogen or (1-4C)alkyl and R^b is hydrogen or (1-4C)alkyl, and wherein any (1-4C)alkyl in R^a or R^b optionally bears one or more substituents (for example 1, 2 or 3) which may be the same or different selected from halogeno and hydroxy and/or optionally a substituent selected from cyano, nitro,

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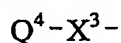
(2-4C)alkenyl, (2-4C)alkynyl, (1-4C)alkoxy, hydroxy(1-4C)alkoxy and (1-2C)alkoxy(1-4C)alkoxy,

or R^a and R^b together with the nitrogen atom to which they are attached form a 4, 5 or 6 membered ring, which optionally bears 1 or 2 substituents, which may be the same or different, on an available ring carbon atom selected from halogeno, hydroxy, (1-4C)alkyl and (1-3C)alkylenedioxy, and may optionally bear on any available ring nitrogen a substituent (provided the ring is not thereby quaternised) selected from (1-4C)alkyl, (2-4C)alkanoyl and (1-4C)alkylsulfonyl,

and wherein any (1-4C)alkyl or (2-4C)alkanoyl group present as a substituent on the ring formed by R^a and R^b together with the nitrogen atom to which they are attached, optionally bears one or more substituents (for example 1, 2 or 3) which may be the same or different selected from halogeno and hydroxy and/or optionally a substituent selected from (1-4C)alkyl and (1-4C)alkoxy;

and wherein any heterocyclyl group Q¹- group optionally bears 1 or 2 oxo (=O) or thioxo (=S) substituents;

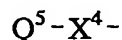
and the other of R^{1a} or R^{1b} is a group R¹ which is selected from hydrogen, hydroxy, (1-6C)alkoxy, (2-6C)alkenyloxy, (2-6C)alkynyloxy, or a group of the formula :



wherein X³ is a direct bond or is selected from O or S, and Q⁴ is (3-7C)cycloalkyl, (3-7C)cycloalkyl-(1-6C)alkyl, (3-7C)cycloalkenyl, (3-7C)cycloalkenyl-(1-6C)alkyl, heterocyclyl or heterocyclyl-(1-6C)alkyl,

and wherein adjacent carbon atoms in any (2-6C)alkylene chain within a R¹ substituent are optionally separated by the insertion into the chain of a group selected from O, S, SO, SO₂, N(R⁴), CO, CH(OR⁴), CON(R⁴), N(R⁴)CO, SO₂N(R⁴), N(R⁴)SO₂, CH=CH and C≡C wherein R⁴ is hydrogen or (1-6C)alkyl,

and wherein any CH₂=CH- or HC≡C- group within a R¹ substituent optionally bears at the terminal CH₂= or HC≡ position a substituent selected from halogeno, carboxy, carbamoyl, (1-6C)alkoxycarbonyl, N-(1-6C)alkylcarbamoyl, N,N-di-[(1-6C)alkyl]carbamoyl, amino-(1-6C)alkyl, (1-6C)alkylamino-(1-6C)alkyl and di-[(1-6C)alkyl]amino-(1-6C)alkyl or from a group of the formula :

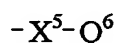


wherein X⁴ is a direct bond or is selected from CO and N(R⁵)CO, wherein R⁵ is hydrogen or (1-6C)alkyl, and Q⁵ is heterocyclyl or heterocyclyl-(1-6C)alkyl,

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and wherein any alkyl or alkylene group within a R¹ substituent optionally bears one or more halogeno, (1-6C)alkyl, hydroxy, cyano, amino, carboxy, carbamoyl, sulfamoyl, (1-6C)alkoxy, (1-6C)alkylthio, (1-6C)alkylsulfinyl, (1-6C)alkylsulfonyl, (1-6C)alkylamino, di-[(1-6C)alkyl]amino, (1-6C)alkoxycarbonyl, N-(1-6C)alkylcarbamoyl,

- 5 N,N-di-[(1-6C)alkyl]carbamoyl, (2-6C)alkanoyl, (2-6C)alkanoyloxy, (2-6C)alkanoylamino, N-(1-6C)alkyl-(2-6C)alkanoylamino, N-(1-6C)alkylsulfamoyl, N,N-di-[(1-6C)alkyl]sulfamoyl, (1-6C)alkanesulfonylamino and N-(1-6C)alkyl-(1-6C)alkanesulfonylamino, or from a group of the formula:



- 10 wherein X⁵ is a direct bond or is selected from O, S, SO, SO₂, N(R⁶), CO, CH(OR⁶), CON(R⁶), N(R⁶)CO, SO₂N(R⁶), N(R⁶)SO₂, C(R⁶)₂O, C(R⁶)₂S and C(R⁶)₂N(R⁶), wherein R⁶ is hydrogen or (1-6C)alkyl, and Q⁶ is (3-7C)cycloalkyl, (3-7C)cycloalkyl-(1-6C)alkyl, (3-7C)cycloalkenyl, (3-7C)cycloalkenyl-(1-6C)alkyl, heterocyclyl or heterocyclyl-(1-6C)alkyl,

- 15 and wherein any heterocyclyl group within a substituent on R¹ optionally bears 1, 2 or 3 substituents, which may be the same or different, selected from halogeno, trifluoromethyl, cyano, nitro, hydroxy, amino, carboxy, carbamoyl, formyl, mercapto, (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl, (1-6C)alkoxy, (2-6C)alkenyloxy, (2-6C)alkynyloxy, (1-6C)alkylthio, (1-6C)alkylsulfinyl, (1-6C)alkylsulfonyl, (1-6C)alkylamino, di-[(1-6C)alkyl]amino, (1-6C)alkoxycarbonyl, N-(1-6C)alkylcarbamoyl, N,N-di-[(1-6C)alkyl]carbamoyl, (2-6C)alkanoyl, (2-6C)alkanoyloxy, (2-6C)alkanoylamino, N-(1-6C)alkyl-(2-6C)alkanoylamino, N-(1-6C)alkylsulfamoyl, N,N-di-[(1-6C)alkyl]sulfamoyl, (1-6C)alkanesulfonylamino, and N-(1-6C)alkyl-(1-6C)alkanesulfonylamino, or from a group of the formula:

- 25 $-X^6-R^7$

wherein X⁶ is a direct bond or is selected from O, N(R⁸) and C(O), wherein R⁸ is hydrogen or (1-6C)alkyl, and R⁷ is halogeno-(1-6C)alkyl, hydroxy-(1-6C)alkyl, carboxy-(1-6C)alkyl, (1-6C)alkoxy-(1-6C)alkyl, cyano-(1-6C)alkyl, amino-(1-6C)alkyl, (1-6C)alkylamino-(1-6C)alkyl, di-[(1-6C)alkyl]amino-(1-6C)alkyl,

- 30 (2-6C)alkanoylamino-(1-6C)alkyl, (1-6C)alkoxycarbonylamino-(1-6C)alkyl, carbamoyl-(1-6C)alkyl, N-(1-6C)alkylcarbamoyl-(1-6C)alkyl, N,N-di-[(1-6C)alkyl]carbamoyl-(1-6C)alkyl, (2-6C)alkanoyl-(1-6C)alkyl or (1-6C)alkoxycarbonyl-(1-6C)alkyl,

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and wherein any heterocyclyl group within a substituent on R¹ optionally bears 1 or 2 oxo or thioxo substituents;

R² is selected from hydrogen and (1-6C)alkyl;

each R³, which may be the same or different, is selected from halogeno, cyano, nitro,
 5 hydroxy, amino, carboxy, carbamoyl, sulfamoyl, trifluoromethyl, (1-6C)alkyl, (2-8C)alkenyl,
 (2-8C)alkynyl, (1-6C)alkoxy, (2-6C)alkenyloxy, (2-6C)alkynyloxy, (1-6C)alkylthio,
 (1-6C)alkylsulfinyl, (1-6C)alkylsulfonyl, (1-6C)alkylamino, di-[(1-6C)alkyl]amino,
 (1-6C)alkoxycarbonyl, N-(1-6C)alkylcarbamoyl, N,N-di-[(1-6C)alkyl]carbamoyl,
N-(1-6C)alkylsulfamoyl, and N,N-di-[(1-6C)alkyl]sulfamoyl

10 a is 1, 2, 3, 4 or 5;

or a pharmaceutically acceptable salt thereof;

subject to the following provisos:

(i) when Q² is aryl, then R^{1a} is a group of sub-formula (i) defined above and R^{1b} is the group R¹ defined above; and

15 (ii) the compound of formula I is not one of the following:

N-(3,4-dichlorophenyl)-7-[(4-[(3,5-dimethylisoxazol-4-yl)carbonyl]morpholin-2-yl)methyl]oxy]-6-(methyloxy)quinazolin-4-amine;

N-(3,4-dichlorophenyl)-7-([4-(furan-3-ylcarbonyl)morpholin-2-yl]methyl)oxy]-6-(methyloxy)quinazolin-4-amine;

20 7-[(4-[(2-chloropyridin-3-yl)carbonyl]morpholin-2-yl)methyl]oxy]-N-(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine; or

7-[(4-[(6-chloropyridin-3-yl)carbonyl]morpholin-2-yl)methyl]oxy]-N-(3,4-dichlorophenyl)-6-(methyloxy)quinazolin-4-amine.

25 2. A quinazoline derivative according to any one of the preceding claims wherein X² is a direct bond.

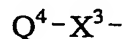
3. A quinazoline derivative according to claim 1 or claim 2, wherein R^{1a} is a group of sub-formula (i), and R^{1b} is a group R¹ as defined in claim 1.

30

4. A quinazoline derivative according to claim 1 or claim 2, wherein R^{1a} is a group R¹, and R^{1b} is a group of sub-formula (i) as defined in claim 1.

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5. A quinazoline derivative according to any one of the preceding claims, wherein R^1 is selected from hydrogen, hydroxy, (1-6C)alkoxy, (2-6C)alkenyloxy, (2-6C)alkynyloxy, or a group of the formula :



- 5 wherein X^3 is a direct bond or is O or S (particularly a direct bond or O), and Q^4 is (3-7C)cycloalkyl, (3-7C)cycloalkyl-(1-6C)alkyl, (3-7C)cycloalkenyl, (3-7C)cycloalkenyl-(1-6C)alkyl, heterocyclyl or heterocyclyl-(1-6C)alkyl, and wherein any alkyl or alkylene group within a R^1 substituent optionally bears one or more halogeno, (1-6C)alkyl, hydroxy, cyano, amino, carboxy, carbamoyl, sulfamoyl, (1-6C)alkoxy, 10 (1-6C)alkylthio, (1-6C)alkylsulfinyl, (1-6C)alkylsulfonyl, (1-6C)alkylamino, di-[(1-6C)alkyl]amino, (1-6C)alkoxycarbonyl, N-(1-6C)alkylcarbamoyl, N,N-di-[(1-6C)alkyl]carbamoyl, (2-6C)alkanoyl, (2-6C)alkanoyloxy, (2-6C)alkanoylamino, N-(1-6C)alkyl-(2-6C)alkanoylamino, N-(1-6C)alkylsulfamoyl, N,N-di-[(1-6C)alkyl]sulfamoyl, (1-6C)alkanesulfonylamino and 15 N-(1-6C)alkyl-(1-6C)alkanesulfonylamino.

6. A quinazoline derivative according to claim 5 wherein R^1 is hydrogen, (1-6C)alkoxy and (1-4C)alkoxy(1-6C)alkoxy, and wherein any (1-6C)alkoxy group within R^1 optionally bears 1, 2 or 3 substituents, which may be the same or different, selected from hydroxy, fluoro 20 and chloro.

7. A quinazoline derivative according to claim 6 wherein R^1 is selected from methoxy, ethoxy, isopropoxy, cyclopropylmethoxy, 2-hydroxyethoxy, 2-fluoroethoxy, 2-methoxyethoxy, 2,2-difluoroethoxy, 2,2,2-trifluoroethoxy or 3-hydroxy-3-methylbutoxy. 25

8. A quinazoline derivative according to claim 5 wherein R^1 is methoxy.

30

9. A quinazoline derivative according to any one of the preceding claims wherein X^1 is suitably a direct bond or a (1-6C)alkylene group.

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10. A quinazoline derivative according to claim 9 wherein X^1 is a direct bond or methylene or ethylene group.

11. A quinazoline derivative according to any one of the preceding claims wherein Z is
5 selected from $-C(O)-$, $-NR^{10}-C(O)-$ (wherein R^{10} is H or (1-6C)alkyl), and $-O-C(O)-$.

12. A quinazoline derivative according to claim 11, wherein Z is $-C(O)-$.

13. A quinazoline derivative according to claim 11, wherein Z is selected from
10 $-NH-C(O)-$ and $-O-C(O)-$.

14. A quinazoline derivative according to any one of the preceding claims wherein Q^1 is a non-aromatic saturated or partially saturated 3 to 10 membered monocyclic heterocyclic ring with up to five heteroatoms selected from oxygen, nitrogen and sulfur (but not containing any
15 O-O, O-S or S-S bonds), and linked via a ring carbon atom, or a ring nitrogen atom (provided the ring is not thereby quaternised).

15. A quinazoline derivative according to any one of the preceding claims wherein Q^1 is selected from oxiranyl, oxetanyl, azetidiny, tetrahydrofuranyl, tetrahydropyranyl, oxepanyl,
20 oxazepanyl, pyrrolinyl, pyrrolidinyl, morpholinyl, tetrahydro-1,4-thiazinyl, 1,1-dioxotetrahydro-1,4-thiazinyl, piperidinyl, homopiperidinyl, piperazinyl, homopiperazinyl, dihydropyridinyl, tetrahydropyridinyl, dihydropyrimidinyl, tetrahydropyrimidinyl, tetrahydrothienyl, tetrahydrothiopyranyl, thiomorpholinyl, more specifically including for example, tetrahydrofuran-3-yl, tetrahydrofuran-2-yl,
25 tetrahydropyran-4-yl, tetrahydrothien-3-yl, tetrahydrothiopyran-4-yl, pyrrolidin-3-yl, pyrrolidin-2-yl, 3-pyrrolin-3-yl, morpholino, 1,1-dioxotetrahydro-4H-1,4-thiazin-4-yl, piperidino, piperidin-4-yl, piperidin-3-yl, piperidin-2-yl, homopiperidin-3-yl, homopiperidin-4-yl, piperazin-1-yl, 1,4-oxazepanyl, or 1,2,3,6-tetrahydropyridin-4-yl.

30 16. A quinazoline derivative according to any one of claims 11 to 16, wherein the group Q^2-X^1-Z- is linked to a nitrogen atom on a heterocyclic atom of Q^1 .

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17. A quinazoline derivative according to any one of the preceding claims, wherein Q² is a heteroaryl group, said heteroaryl group being optionally substituted by one of more substituents selected from halogeno, trifluoromethyl, trifluoromethoxy, cyano, nitro, hydroxy, amino, carboxy, carbamoyl, acryloyl, (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl, (1-6C)alkoxy, (2-6C)alkenyloxy, (2-6C)alkynyloxy, (1-6C)alkylthio, (2-6C)alkenylthio, (2-6C)alkynylthio, (1-6C)alkylsulfinyl, (2-6C)alkenylsulfinyl, (2-6C)alkynylsulfinyl, (1-6C)alkylsulfonyl, (2-6C)alkenylsulfonyl, (2-6C)alkynylsulfonyl, (1-6C)alkylamino, di-[(1-6C)alkyl]amino, (1-6C)alkoxycarbonyl, N-(1-6C)alkylcarbamoyl, N,N-di-[(1-6C)alkyl]carbamoyl, (2-6C)alkanoyl, (2-6C)alkanoyloxy, (2-6C)alkanoylamino, N-(1-6C)alkyl-(2-6C)alkanoylamino, sulfamoyl, N-(1-6C)alkylsulfamoyl, N,N-di-[(1-6C)alkyl]sulfamoyl, (1-6C)alkanesulfonylamino, N-(1-6C)alkyl-(1-6C)alkanesulfonylamino, carbamoyl(1-6C)alkyl, N-(1-6C)alkylcarbamoyl(1-6C)alkyl, N,N-di-[(1-6C)alkyl]carbamoyl(1-6C)alkyl, sulfamoyl(1-6C)alkyl, N-(1-6C)alkylsulfamoyl(1-6C)alkyl, N,N-di-[(1-6C)alkyl]sulfamoyl(1-6C)alkyl, (2-6C)alkanoyl(1-6C)alkyl, (2-6C)alkanoyloxy(1-6C)alkyl, (2-6C)alkanoylamino(1-6C)alkyl, N-(1-6C)alkyl-(2-6C)alkanoylamino(1-6C)alkyl and (1-6C)alkoxycarbonyl(1-6C)alkyl, and wherein any (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl and (2-6C)alkanoyl substituent on Q² optionally bears one or more substituents (for example 1, 2 or 3) which may be the same or different selected from halogeno, hydroxy and (1-6C)alkyl and/or optionally a substituent selected from cyano, nitro, carboxy, (2-8C)alkenyl, (2-8C)alkynyl, (1-6C)alkoxy, hydroxy(1-6C)alkoxy, (1-4C)alkoxy(1-6C)alkoxy, (2-6C)alkanoyl, (2-6C)alkanoyloxy and NR^aR^b, wherein R^a is hydrogen or (1-4C)alkyl and R^b is hydrogen or (1-4C)alkyl, and wherein any (1-4C)alkyl in R^a or R^b optionally bears one or more substituents (for example 1, 2 or 3) which may be the same or different selected from halogeno and hydroxy and/or optionally a substituent selected from cyano, nitro, (2-4C)alkenyl, (2-4C)alkynyl, (1-4C)alkoxy, hydroxy(1-4C)alkoxy and (1-2C)alkoxy(1-4C)alkoxy, or R^a and R^b together with the nitrogen atom to which they are attached form a 4, 5 or 6 membered ring, which optionally bears 1 or 2 substituents, which may be the same or different, on an available ring carbon atom selected from halogeno, hydroxy, (1-4C)alkyl and (1-3C)alkylenedioxy, and may optionally bear on any available ring nitrogen a substituent (provided the ring is not thereby quaternised) selected from (1-4C)alkyl, (2-4C)alkanoyl and (1-4C)alkylsulfonyl,

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and wherein any (1-4C)alkyl or (2-4C)alkanoyl group present as a substituent on the ring formed by R^a and R^b together with the nitrogen atom to which they are attached, optionally bears one or more substituents (for example 1, 2 or 3) which may be the same or different selected from halogeno and hydroxy and/or optionally a substituent selected from
5 (1-4C)alkyl and (1-4C)alkoxy.

18. A quinazoline derivative according to any one of the preceding claims, wherein Q² is a 5 or 6 membered heteroaryl ring which optionally contains one or more heteroatoms selected from oxygen, nitrogen or sulphur.

10

19. A quinazoline derivative according to claim 18 wherein Q² is selected from furyl, thienyl, pyrrolyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, 1,2,3-triazolyl, 1,2,4-triazolyl, oxadiazolyl, furazanyl, thiadiazolyl or tetrazolyl.

15 20. A quinazoline derivative according to any one of claims 1 to 17, wherein Q² is a 9 or 10 membered bicyclic heteroaryl ring system which optionally contains one or more heteroatoms selected from oxygen, nitrogen or sulphur.

21. A quinazoline derivative according to claim 20, wherein Q² is selected from
20 quinolinyl, isoquinolinyl, cinnolinyl, quinazolinyl, phthalazinyl, quinoxalinyl, indolyl, isoindolyl, benzofuranyl, benzothienyl, benzimidazolyl, benzothiazolyl or purinyl.

22. A quinazoline derivative according to any one of claims 1 to 16, wherein Q² is an aryl group selected from phenyl and naphthyl.

25

23. A quinazoline derivative according to any one of the preceding claims wherein Q² optionally bears 1 or 2 substituents, which may be the same or different, selected from halogeno, hydroxy, nitro, amino, cyano, carbamoyl, (1-4C)alkyl, (1-4C)alkoxy, (2-4C)alkanoyl and (1-4C)alkylsulfonyl, (1-4C)alkylamino, di[(1-4C)alkyl]amino, N-[(1-
30 4C)alkyl]carbamoyl, and N,N-di[(1-4C)alkyl]carbamoyl.

and wherein any (1-4C)alkyl, or (2-4C)alkanoyl group within Q² optionally bears 1 or 2 substituents, which may be the same or different, selected from halogeno, hydroxy and (1-6C)alkyl and/or optionally a substituent selected from cyano, (2-8C)alkenyl,

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(2-8C)alkynyl, (1-6C)alkoxy, (2-6C)alkanoyl, (2-6C)alkanoyloxy and NR^aR^b , wherein R^a is hydrogen or (1-4C)alkyl and R^b is hydrogen or (1-4C)alkyl, and wherein any (1-4C)alkyl in R^a or R^b optionally bears one or more substituents (for example 1, 2 or 3) which may be the same or different selected from halogeno and hydroxy and/or optionally a substituent selected
5 from cyano, and (1-4C)alkoxy,

or R^a and R^b together with the nitrogen atom to which they are attached form a 4, 5 or 6 membered ring which does not contain oxygen, which ring optionally bears 1 or 2 substituents, which may be the same or different, on an available ring carbon atom selected from halogeno, hydroxy, (1-4C)alkyl and (1-3C)alkylenedioxy, and may optionally bear on
10 any available ring nitrogen a substituent (provided the ring is not thereby quaternised) selected from (1-4C)alkyl, (2-4C)alkanoyl and (1-4C)alkylsulfonyl,

and wherein any (1-4C)alkyl or (2-4C)alkanoyl group present as a substituent on the ring formed by R^a and R^b together with the nitrogen atom to which they are attached optionally bears one or more substituents (for example 1, 2 or 3), which may be the same or
15 different, selected from halogeno and hydroxy and/or optionally a substituent selected from (1-4C)alkyl and (1-4C)alkoxy.

24. A quinazoline derivative according to claim 23 wherein Q^2 is optionally substituted by one or two groups, which may be the same or different, selected from halogeno, hydroxy,
20 nitro, amino, cyano, carbamoyl, (1-4C)alkyl, (1-4C)alkoxy, (2-4C)alkanoyl and (1-4C)alkylsulfonyl, [(1-4C)alkyl]amino, di[(1-4C)alkyl]amino, *N*-[(1-4C)alkyl]carbamoyl, and *N,N*-di[(1-4C)alkyl]carbamoyl.

and wherein any (2-4C)alkanoyl group in a substituent on Q^2 optionally bears one or two substituents, which may be the same or different, selected from hydroxy and (1-3C)alkyl,
25 and wherein any (1-4C)alkyl group in a substituent on Q^2 optionally bears one or two substituents, which may be the same or different, selected from hydroxy, (1-4C)alkoxy and halogeno (particularly chloro and more particularly fluoro).

25. A quinazoline derivative according to claim 23 or claim 24 wherein Q^2 is
30 unsubstituted or substituted by a (1-4C)alkyl group, a (1-4C)alkoxy group, halogeno, amino, nitro, cyano, carbamoyl, di-[(1-4C)alkyl]amino, and *N,N*-di[(1-4C)alkyl]carbamoyl.

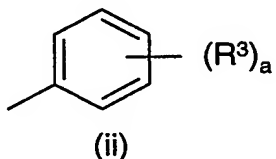
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26. A quinazoline derivative according to any one of the preceding claims wherein R^2 is hydrogen.

27. A quinazoline derivative according to any one of the preceding claims wherein a is 1,
5 2 or 3.

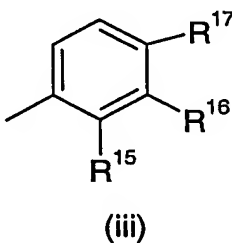
28. A quinazoline derivative according to any one of the preceding claims, wherein an R^3 is in the para position on the anilino ring, and this is selected from halogeno, cyano, nitro, hydroxy, amino, trifluoromethyl, (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl, (1-6C)alkoxy,
10 (2-6C)alkenyloxy, (2-6C)alkynyloxy, (1-6C)alkylthio, (1-6C)alkylamino and di-[(1-6C)alkyl]amino.

29. A quinazoline derivative according to any one of the preceding claims wherein the group of sub-formula (ii)



15

in formula (I) is a group of sub-formula (iii)



where one of R^{15} or R^{17} is hydrogen and the other is halogeno, and R^{16} is halogeno.

20 30. A quinazoline derivative according to claim 29 wherein the group of sub-formula (iii) is 3-chloro-2-fluorophenyl, or 3-chloro-4-fluorophenyl.

31. A compound selected from one of the following:

- 25 (1) *N*-(3-chloro-2-fluorophenyl)-6-([1-(isoxazol-5-ylcarbonyl)piperidin-4-yl]oxy)-7-methoxyquinazolin-4-amine;
- (2) *N*-(3-chloro-2-fluorophenyl)-7-methoxy-6-([1-[(3-methylisoxazol-5-yl)acetyl]piperidin-4-yl]oxy)quinazolin-4-amine;

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- (3) *N*-(3-chloro-2-fluorophenyl)-7-methoxy-6-({1-[(3-methylisoxazol-5-yl)carbonyl]piperidin-4-yl}oxy)quinazolin-4-amine;
- (4) *N*-(3-chloro-2-fluorophenyl)-7-methoxy-6-({1-[(5-methylisoxazol-3-yl)carbonyl]piperidin-4-yl}oxy)quinazolin-4-amine;
- 5 (5) *N*-(3-chloro-2-fluorophenyl)-7-methoxy-6-({1-[(5-methylisoxazol-4-yl)carbonyl]piperidin-4-yl}oxy)quinazolin-4-amine;
- (6) *N*-(3-chloro-2-fluorophenyl)-7-methoxy-6-({1-[(3-methylisoxazol-4-yl)carbonyl]piperidin-4-yl}oxy)quinazolin-4-amine;
- (7) *N*-(3-chloro-2-fluorophenyl)-6-({1-[(3,5-dimethylisoxazol-4-yl)carbonyl]piperidin-4-yl}oxy)-7-methoxyquinazolin-4-amine;
- 10 (8) *N*-(3-chloro-2-fluorophenyl)-7-methoxy-6-{[1-(pyridin-3-ylcarbonyl)piperidin-4-yl]oxy}quinazolin-4-amine;
- (9) *N*-(3-chloro-2-fluorophenyl)-7-methoxy-6-{[1-(pyridin-2-ylcarbonyl)piperidin-4-yl]oxy}quinazolin-4-amine;
- 15 (10) *N*-(3-chloro-2-fluorophenyl)-6-{[1-(2-furoyl)piperidin-4-yl]oxy}-7-methoxyquinazolin-4-amine;
- (11) *N*-(3-chloro-2-fluorophenyl)-7-{[1-(isoxazol-5-ylcarbonyl)piperidin-4-yl]oxy}-6-methoxyquinazolin-4-amine;
- (12) *N*-(3-chloro-2-fluorophenyl)-6-methoxy-7-({1-[(3-methylisoxazol-5-yl)acetyl]piperidin-4-yl}oxy)quinazolin-4-amine;
- 20 (13) *N*-(3-chloro-2-fluorophenyl)-7-{[1-(pyridin-3-ylcarbonyl)piperidin-4-yl]oxy}-6-methoxyquinazolin-4-amine;
- (14) *N*-(3-chloro-2-fluorophenyl)-7-{[1-(2-furoyl)piperidin-4-yl]oxy}-6-methoxyquinazolin-4-amine;
- (15) *N*-(3-chloro-2-fluorophenyl)-7-methoxy-6-{[(3*R*)-1-(2-thienylacetyl)piperidin-3-yl]oxy}quinazolin-4-amine;
- 25 (16) *N*-(3-chloro-2-fluorophenyl)-6-{[(3*R*)-1-isonicotinoylpiperidin-3-yl]oxy}-7-methoxyquinazolin-4-amine;
- (17) 6-({(3*R*)-1-[(2-aminopyridin-3-yl)carbonyl]piperidin-3-yl}oxy)-*N*-(3-chloro-2-fluorophenyl)-7-methoxyquinazolin-4-amine;
- 30 (18) *N*-(3-chloro-2-fluorophenyl)-7-methoxy-6-{[(3*R*)-1-(1*H*-pyrrol-2-ylcarbonyl)piperidin-3-yl]oxy}quinazolin-4-amine;

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- (19) *N*-(3-chloro-2-fluorophenyl)-7-methoxy-6-{[(3*R*)-1-(2-thienylcarbonyl)piperidin-3-yl]oxy}quinazolin-4-amine;
- (20) *N*-(3-chloro-2-fluorophenyl)-6-{[(3*R*)-1-(2-furoyl)piperidin-3-yl]oxy}-7-methoxyquinazolin-4-amine;
- 5 (21) *N*-(3-chloro-2-fluorophenyl)-6-{[(3*R*)-1-(3-furoyl)piperidin-3-yl]oxy}-7-methoxyquinazolin-4-amine;
- (22) *N*-(3-chloro-2-fluorophenyl)-7-methoxy-6-{[(3*R*)-1-(3-thienylcarbonyl)piperidin-3-yl]oxy}quinazolin-4-amine;
- (23) *N*-(3-chloro-2-fluorophenyl)-7-methoxy-6-{[(3*R*)-1-(3-thienylacetyl)piperidin-3-yl]oxy}quinazolin-4-amine;
- 10 (24) *N*-(3-chloro-2-fluorophenyl)-7-methoxy-6-({(3*R*)-1-[(1-methyl-1*H*-pyrrol-2-yl)carbonyl]piperidin-3-yl}oxy)quinazolin-4-amine;
- (25) *N*-(3-chloro-2-fluorophenyl)-7-methoxy-6-({(3*R*)-1-[(4-nitro-1*H*-pyrazol-1-yl)acetyl]piperidin-3-yl}oxy)quinazolin-4-amine;
- 15 (26) *N*-(3-chloro-2-fluorophenyl)-7-methoxy-6-({(3*R*)-1-[(3-methylisoxazol-5-yl)acetyl]piperidin-3-yl}oxy)quinazolin-4-amine;
- (27) *N*-(3-chloro-2-fluorophenyl)-7-methoxy-6-{[(3*R*)-1-(4-{*N,N*-dimethylcarbamoyl}-1*H*-pyrazol-1-yl)acetyl]piperidin-3-yl]oxy}quinazolin-4-amine;
- 20 (28) *N*-(3-chloro-2-fluorophenyl)-7-methoxy-6-{[(3*R*)-1-(4-cyano-1*H*-pyrazol-1-yl)acetyl]piperidin-3-yl]oxy}quinazolin-4-amine;
- (29) 4-({4-[(3-Chloro-2-fluorophenyl)amino]-7-methoxyquinazolin-6-yl}oxy)-*N*-phenylpiperidine-1-carboxamide;
- (30) *N*-Benzyl-4-({4-[(3-chloro-2-fluorophenyl)amino]-7-methoxyquinazolin-6-yl}oxy)piperidine-1-carboxamide;
- 25 (31) 4-({4-[(3-Chloro-2-fluorophenyl)amino]-7-methoxyquinazolin-6-yl}oxy)-*N*-[4-(dimethylamino)phenyl]piperidine-1-carboxamide;
- (32) 4-({4-[(3-Chloro-2-fluorophenyl)amino]-7-methoxyquinazolin-6-yl}oxy)-*N*-(2-phenylethyl)piperidine-1-carboxamide;
- 30 (33) 4-({4-[(3-Chloro-2-fluorophenyl)amino]-7-methoxyquinazolin-6-yl}oxy)-*N*-(3,4-dimethoxyphenyl)piperidine-1-carboxamide;
- (34) 4-({4-[(3-Chloro-2-fluorophenyl)amino]-7-methoxyquinazolin-6-yl}oxy)-*N*-(3-fluorophenyl)piperidine-1-carboxamide;

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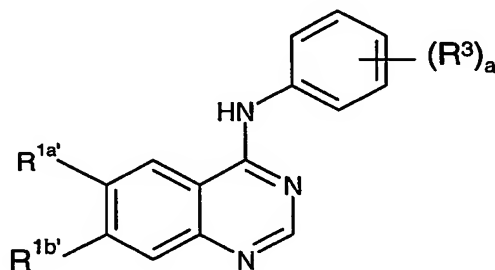
(35) 4-({4-[(3-Chloro-2-fluorophenyl)amino]-7-methoxyquinazolin-6-yl}oxy)-
N-(3,5-dimethylisoxazol-4-yl)piperidine-1-carboxamide;

(36) 4-({4-[(3-Chloro-2-fluorophenyl)amino]-7-methoxyquinazolin-6-yl}oxy)-
N-2-thienylpiperidine-1-carboxamide;

5 (37) 4-({4-[(3-chloro-2-fluorophenyl)amino]-7-methoxyquinazolin-6-yl}oxy)-
N-3-thienylpiperidine-1-carboxamide.

32. A process for the preparation of a quinazoline derivative of the Formula I as defined in any one of the preceding claims, which process comprises either

10 **Process (a)** reacting a compound of the Formula II:



Formula II

15 wherein R³ and a are as defined in claim 1 and one of R^{1a'} or R^{1b'} is hydroxy and the other is a group R¹ as defined in claim 1 in relation to formula (I), except that any functional group is protected if necessary,
with a compound of the Formula III:



20 Formula III

wherein Q¹, Q², Z, X² and X¹ have any of the meanings defined in claim 1, except that any functional group is protected if necessary and Lg is a displaceable group:

Process (b) modifying a substituent in or introducing a substituent into another quinazoline derivative of Formula I or a pharmaceutically acceptable salt thereof as defined in claim 1,

25 except that any functional group is protected if necessary;

Process (c) reacting a compound of the Formula II as defined in respect of process (a) above with a compound of the Formula III as defined in process (a) except Lg is OH under Mitsunobu conditions,

Process (d) for the preparation of those compounds of the Formula I wherein the group R¹

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is a hydroxy group by the cleavage of a quinazoline derivative of the Formula I wherein R^1 is a (1-6C)alkoxy group;

Process (e) for the preparation of those compounds of the Formula I wherein R^1 is a (1-6C)alkoxy, (2-6C)alkenyloxy, (2-6C)alkynyloxy, or a group of the formula :



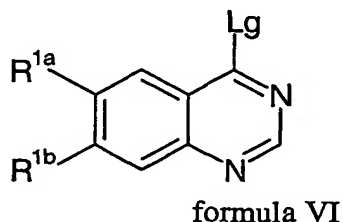
wherein X^3 is O and Q^4 is as defined in claim 5, by the reaction of a compound of the Formula I wherein R^1 is OH, except that any functional group is protected if necessary, with a compound of the formula $R^{1'}-Lg$, wherein $R^{1'}$ is a (1-6C)alkyl, (2-6C)alkenyl, (2-6C)alkynyl, or a group Q^4 where Q^4 is as defined in claim 5, and Lg is a displaceable group;

10 **Process (f)** for the preparation of those compounds of the Formula I wherein Q^1 , Q^2 contains or R^1 is or contains a (1-6C)alkoxy or substituted (1-6C)alkoxy group or a (1-6C)alkylamino or substituted (1-6C)alkylamino group, the alkylation of a quinazoline derivative of the Formula I wherein Q^1 , Q^2 contains or R^1 is or contains a hydroxy group or a primary or secondary amino group as appropriate;

15 **Process (g)** for the preparation of those compounds of the Formula I wherein R^1 is substituted by a group T, wherein T is selected from (1-6C)alkylamino, di-[(1-6C)alkyl]amino, (2-6C)alkanoylamino, (1-6C)alkylthio, (1-6C)alkylsulfinyl and (1-6C)alkylsulfonyl, the reaction of a compound which is of formula (I) except that the group R^1 is replaced with a group $R^{1''}-Lg$ wherein Lg is a displaceable group, and $R^{1''}$ is a group R^1

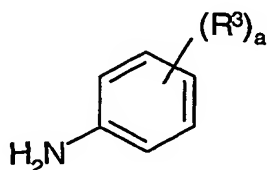
20 except that it has Lg in place of the group T, and further that any functional group is protected if necessary, with a compound of the formula TH, wherein T is as defined above except that any functional group is protected if necessary;

Process (h) by reacting a compound of the formula VI:



25

wherein R^{1a} and R^{1b} have any of the meanings defined in claim 1 except that any functional group is protected if necessary and Lg is a displaceable group, with an aniline of the formula VII:



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formula VII

wherein R^3 and a have any of the meanings defined in claim 1, except that any functional group is protected if necessary, and wherein the reaction is conveniently performed in the presence of a suitable acid, or

- 5 **Process (i)** for the preparation of those compounds of the Formula I wherein Q^1 is a nitrogen containing heterocyclyl group linked to the group Z by a ring nitrogen, the coupling of a compound of the Formula I as defined in claim 1, except that the group of sub-formula (i) is a group of sub-formula (x) $H-Q^1-X^2-O-$, and any functional group is protected if necessary, with a compound of formula Q^2-X^1-Z-Lg , wherein Z, Q^2 and X^1 are as defined in claim 1 and

10 Lg is a leaving group;

- Process (j)** for the preparation of those compounds of the Formula I define in claim 1 wherein Q^1 is a nitrogen containing heterocyclyl group linked to the -Z- group by a ring nitrogen, and Z is a group of formula $-NR^{10}-C(O)-$; said process comprising the coupling of a compound of the Formula I, except that the group of sub-formula (i) is a group of sub-formula
- 15 (x) $H-Q^1-X^2-O-$, and any functional group is protected if necessary, with a compound of formula $Q^2-X^1-N=C=O$, wherein Q^2 and X^1 are as defined in claim 1; and whereafter any protecting group that is present is removed by conventional means.

33. A process according to claim 32, wherein Lg is a leaving group selected from
- 20 hydroxyl, chloro or bromo.

34. A pharmaceutical composition which comprises a quinazoline derivative of the Formula I, or a pharmaceutically-acceptable salt thereof, as defined in any one of claims 1 to 31 in association with a pharmaceutically-acceptable diluent or carrier.

25

35. A quinazoline derivative of the Formula I as defined in any one of claims 1 to 31, or a pharmaceutically acceptable salt thereof, for use as a medicament.

36. The use of a quinazoline derivative of the Formula I, or a pharmaceutically-acceptable
- 30 salt thereof, as defined in any one of claims 1 to 31 in the manufacture of a medicament for use in the production of an anti-proliferative effect in a warm-blooded animal.

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37. A method for producing an anti-proliferative effect in a warm-blooded animal in need of such treatment which comprises administering to said animal a quinazoline derivative of the Formula I, or a pharmaceutically acceptable salt thereof, as defined in any one of claims 1 to 31.

5